UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,290	01/11/2007	Robert Edward Coleman	33540-US-PCT	2763

1095 7590 12/07/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	**PAPER NUMBER**
1612	
MAIL DATE	**DELIVERY MODE**
12/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,290	COLEMAN ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,11-13,26 and 28-31* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,11,26 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page 11/25/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on November 25, 2009.

Receipt of Declarations under 37 CFR 1.132 is acknowledged.

Status of Claims

Claims 7, 11-13, 26 and 28-31 are currently pending and are the subject of this office action.

Claims 12 and 13 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on January 25, 2008

Claims 7, 11, 26 and 28-31 are presently under examination.

The following species is currently under examination: paclitaxel (PAC) as the chemotherapeutic agent.

Priority

The present application is a 371 of PCT/EP04/13728 filed on 12/02/2004, and claims priority to foreign application: UNITED KINGDOM No. 0328040 filed on 08/04/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated

(Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (Maintained Rejection)

Claims 7, 11, 26 and 28 and new claims 29-31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Jagdev et. al. (British Journal of Cancer (2001) 84:1126-1134).

The reasons for this rejection have been provided in the previous office action dated June 17, 2009 the text of which is incorporated by reference herein.

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that:

Applicant basically presents similar arguments as presented in previous replies: that the dose regimen of the instant application:

treatment of MCF7 cells with:

1- 2 nM PAC (for 4 hours on day 1) followed by 25 μ ZOL (for 1 hour on day 2) (see Experiment 1 on page 15 of the specification), or

2- 2nM PAC (for 4 hours on day 1) followed by 1 μM ZOL (for 1 hour on day 2) (see Experiment 2 on page 15 of the specification) show unexpected synergistic results that would have not been expected from the data provided by Jagdev:

treatment of MCF7 cells with:

different mixtures of PAC (0 to 10 nM) and ZOL (0 to 100 μM) for 72 hours;

and that the dose regimen of the instant application reflects a true "effective therapeutic dose" as opposed to Jagdev, since it is well known that ZOL has significant toxicity and a short half-life, making the 72 hour exposure of Jagdev unrealistic for clinical use and making impossible to predict whether the therapeutic effects observed after 72 hours exposure may be obtained under clinical conditions. Repeated and prolonged infusion periods of ZOL would be required to reproduce the 72 hours exposure tested by Jagdev and such an exposure is not achievable in clinical practice due to the toxicity of ZOL. By definition, if the concentrations and exposure time of the ZOL disclosed by Jagdev are not clinically achievable, they are not an effective amount as recited by the claimed methods and it is not predictable whether a much shorter exposure time would produce the same synergistic effects.

Examiner's response:

First: there is nothing in the claims that says for how long the patient is being exposed to the combination of ZOL and PAC. So the only difference between what is claimed and the prior art is the sequence of administration: Jagdev administered ZOL and PAC simultaneously, while the instant claims recite the administration in separate days. This difference alone can not warrant novelty, since the skilled in the art will be

able to adjust any *in vitro* regimen to an *in vivo* regimen according to efficacy, toxicity and the and pharmacokinetic properties of a particular drug, and thus obtain an efficacious dose regimen.

Second: even if Applicant had claimed a different exposure time of PAC and ZOL, there is still no proof that the *in vitro* regimen disclosed by Applicant in the specification will actually translate in a better human dose regimen than Jadgev, since neither the Applicant nor Jadgev have presented human data. So Applicant's arguments that the instant *in vitro* dose regimen will translate in a "therapeutically effective dose" as opposed to Jadgev regimen, which according to Applicant is "not clinically achievable" is a mere speculation at this point.

Third: even if *arguendo*, Applicant's prediction were correct, since Jagdev already teaches that this mixture is synergistic *in vitro* when breast cancer cells (MCF7) are exposed for 72 hours to different ratios of PAC and ZOL, and since it is already known in the prior art that ZOL has a short half life and high toxicity, as disclosed by Applicant, the skilled in the art would have been able to adapt the *in vitro* regimen of Jadgev to an *in vivo* regimen that is effective and well tolerated by the patient. As taught by Goodman and Gilman's (The Pharmacological Basis of Therapeutics (Tenth Edition (2001), McGraw Hill, pages 24-29, cited as evidentiary purposes and not as part of the rejection itself) dose regimen optimization is routine in the pharmaceutical art. For example on pages 27 and 28 under the heading: Individualizing dosage, the authors mention that: "A rational dosage regimen is based on knowledge of pharmacokinetic parameters (F, CL, Vss and t1/2) and some information about rates of absorption and

distribution of the drug". They also teach: "Individualization of the dosage regimen to a particular patient is, therefore, critical for optimal therapy. The pharmacokinetic principles, described above, provide a basis for modifying the dosage regimen to obtain a desired degree of efficacy with a minimum of unacceptable adverse effects."

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
December 3, 2009

/Gollamudi S Kishore/

Primary Examiner, Art Unit 1612